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Case Report

Unexpected diagnosis of uterine perivascular epithelioid cell tumors: a case report

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ABSTRACT

Uterine perivascular epithelioid cell tumor (PEComa) is a rare mesenchymal tumor. Most PEComas are benign and patients have good prognosis but sometimes they can have aggressive malignant and metastatic potential. Symptoms are nonspecific and similar to those of other uterine tumors. Correct preoperative diagnosis is rarely achieved due to the presence of nonspecific imaging features. At the present time, surgery is the main treatment and adjuvant chemotherapy is used in malignant cases, with different prognosis for each individual case. This case report describes a 42-year-old Caucasian woman presenting to us with a suspected intramural uterine fibroid, menometrorrhagia and iron deficiency anemia (IDA). At the last check-up, an increase in the volume of the known fibroid was observed on transvaginal ultrasound, which measured 72.6×46.8×70.8 mm. The patient underwent a laparotomic myomectomy for suspected enlarged uterine leiomyoma with elevated tumor markers (LDH and CA-125). Histological examination of the surgical specimen revealed a PEComa of uncertain malignant potential. Following this diagnosis, a total hysterectomy with bilateral adnexectomy was performed with histological examination that confirmed the radicalization of the previous surgery without residual tumor tissue. PEComas of the uterus are rare mesenchymal neoplasms that pose significant diagnostic challenges pre-operatively due to their nonspecific imaging features and no specific Blood Markers. This underscores the importance of including PEComa in the differential diagnosis of uterine tumors to ensure optimal surgical planning and patient outcomes.

Keywords: Uterine perivascular epithelioid cell tumor, PEComa, Differential diagnosis, Rare case, Overlapping, Uterine tumor

INTRODUCTION

Uterine perivascular epithelioid cell tumor (PEComa) is a rare mesenchymal tumor composed of spindle cells which exhibits immunohistochemical co-expressions of melanocytic markers and smooth muscle markers. Most PEComas are benign and patients have good prognosis but sometimes they can have aggressive malignant and metastatic potential. The second most common affected organ is the uterus, after the kidney. PEComa of the female gynecological tract is a rare entity presenting with variable symptoms and some patients may be asymptomatic; Symptoms are nonspecific and similar to those of other uterine tumors.[1]

Correct preoperative diagnosis is rarely achieved due to the presence of nonspecific imaging features; the best diagnostic and management method is yet to be discovered considering the rarity of this neoplasm. At the present time,

surgery is the main treatment and adjuvant chemotherapy is used in malignant cases, with different prognosis for each individual case.[2]

In this case report, a patient with uterine PEComa is reported and described.

Uterine PEComas may show overlapping morphology and immunohistochemistry with uterine smooth muscle tumors. Preoperative discrimination between benign leiomyoma and MMT/STUMP is challenging.

Uterine leiomyomas are the most frequently encountered benign myomatous tumors of the uterus, being observed in up to 20-40% of women of reproductive age and in 70-80% of perimenopausal women. In the malignant spectrum, uterine sarcomas include leiomyosarcoma and other even rarer forms such as endometrial stromal sarcoma, adenosarcoma and undifferentiated sarcoma.

Uterine fibromatosis is not a pathological condition that always requires treatment, but only when it gives rise to symptoms.

The management of fibroids includes three main care approaches: the first, which proposes a wait-and-see attitude with ultrasound checks every 6-12 months to monitor any growth over time. Such management is appropriate for fibroids that do not show a significant tendency to grow and are oligosymptomatic or completely asymptomatic. A second, which includes pharmacological therapy with drugs capable of controlling the symptoms with a specific action on the endometrium such as estro-progestins and progestins, or on both the fibroids and the endometrium inducing a menopause-like state, such as GnRH analogues. A third that considers surgical treatment in various forms.

Alongside these strategies, there are others that are considered "alternative", such as embolization of the uterine arteries and treatment with focused ultrasound guided by magnetic resonance imaging.

These therapeutic paths must be clearly explained and agreed upon with the patient, considering the age, position and number of fibroids, the presence of concomitant pathologies, any previous therapeutic failures and the desire for motherhood.

Because a suspected leiomyoma is often managed conservatively or with minimally invasive treatments, misdiagnosing leiomyosarcoma for a benign leiomyoma could potentially result in significant delays in treatment, thereby increasing morbidity and mortality.[3-5]

CASE REPORT

This case report describes a 42-year-old Caucasian woman presenting to us with a suspected intramural uterine fibroid, menometrorrhagia and iron deficiency anemia (IDA) under treatment with iron supplements. The patient underwent excision of a melanoma in situ in 2017. She also has a thyroid nodule under follow-up and obstetric history of caesarean section in 2019.

The patient has been under annual gynecological examination and ultrasound follow-up for this suspected intramural uterine fibroid. At the last check-up, an increase in the volume of the known fibroid was observed, measuring 72.6×46.8×70.8 mm in a uterus approximately 116.8 mm in length. Consequently, the patient underwent pelvic magnetic resonance imaging (MRI) and blood tests for tumor markers CA-125 and LDH. Magnetic resonance imaging (MRI) revealed a moderately enlarged intramural formation in the anterior wall of the uterine body, measuring 78 mm in diameter, with increased signal heterogeneity and degenerative areas, small fluid collection in the Douglas pouch and no lymphadenopathy. The endometrium appeared thin and unaltered, with an intact junctional zone. The adnexa were normal. Tumor markers were elevated, with LDH at 145 U/l and CA-125 at 61.74 U/ml.

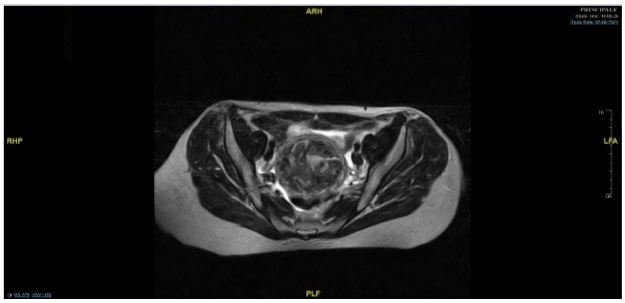

Figure 1: MRI of the pelvis (DEFS T2 TRS).

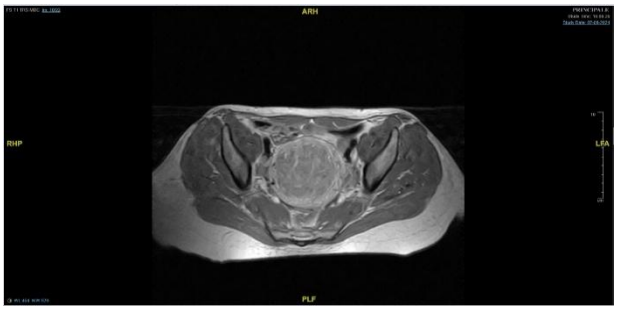

Figure 2: MRI of the pelvis (FS T1 TRS MDC).

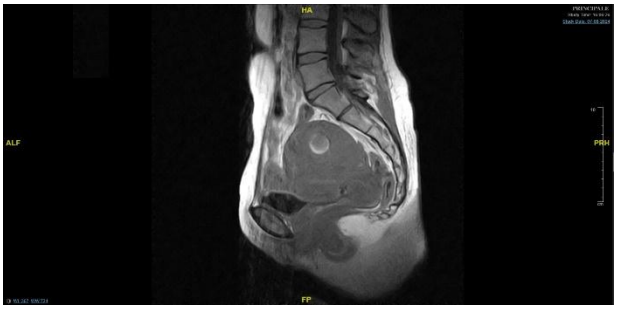

Figure 3: MRI of the pelvis (FS T1 SAG).

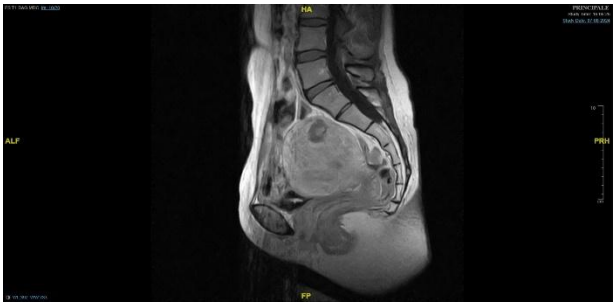

Figure 4: MRI of the pelvis (FS T1 SAG MDC).

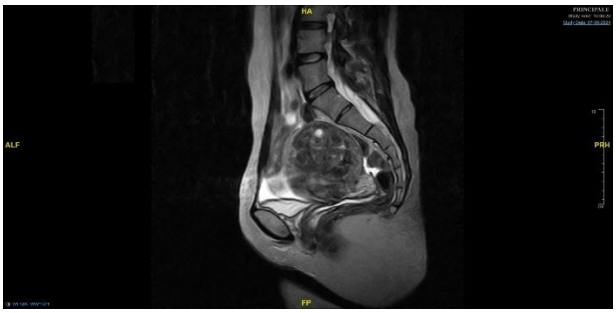

Figure 5: MRI of the pelvis (T2 SAG).

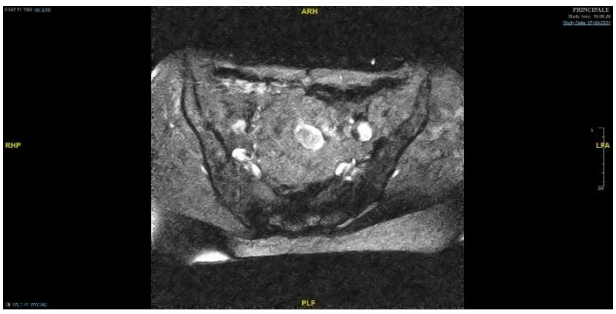

Figure 6: MRI of the pelvis (FSAT T1 TRS).

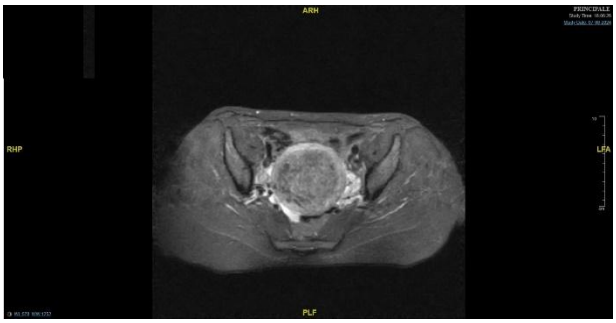

Figure 7: RMI of the Pelvis (STIR TRS).

The patient underwent a laparotomic myomectomy for suspected enlarged uterine leiomyoma with elevated tumor markers. Histological examination of the surgical specimen revealed a 7 cm nodular neoplasm composed of epithelioid cells with clear/eosinophilic cytoplasm, moderate nuclear atypia, organized in solid nests and trabeculae and embedded in a sclerohyaline stroma. No areas of tumor necrosis were observed. A pseudocystic area indicative of recent and past hemorrhage was present. Mitoses were 1-2 per 50 high-power fields (HPFs). The neoplastic cells were positive for SMA, caldesmon, desmin, ER (70%, score 2+/3+), PgR (70%, score 2+/3+), CKAE1/AE3, CK8/18, cathepsin K, CD99, and focally for HMB45, claretinin, and CD10. They were negative for inhibin, GATA3, Melan-A, MIFT, S100, with preserved FH staining and weak TFE3 staining. The endometrium was secretory. The histological diagnosis was a mesenchymal neoplasm with an epithelioid cell profile, compatible with PEComa of uncertain malignant potential.

Following this diagnosis, a total hysterectomy with bilateral adnexectomy was performed. The histological examination confirmed the radicalization of the previous surgery with no neoplastic residues in the uterus.

DISCUSSION

Myometrial pathology includes a variety of conditions that may present with similar symptoms but require different diagnostic and therapeutic approaches. In this context, a distinction can be made between benign and malignant myometrial pathology. The most frequent benignant myometrial pathology is Uterine fibroid which affects the younger population with the need to consider, if required, fertility sparing therapeutic strategies. Malignant pathology, on the other hand, although rare, generally presents in a very aggressive form that requires a targeted therapeutic approach. Understanding the distinctive features of each condition is therefore essential for adequate differential diagnosis and optimal patient management.

The main elements that can be used for a correct diagnostic and therapeutic process are clinical, instrumental and histological features.

Clinical features indicative of malignancy may include abnormal and excessive uterine bleeding, persistent and non-cyclic pelvic pain, rapid increase in the size of the myometrial mass and increased blood levels of the tumor markers LDH and CA-125.[6,7]

Ultrasound is usually the first imaging modality used for the detection of uterine myometrial pathology, it is a crucial tool in this evaluation, providing detailed images that help distinguish between benign and malignant conditions, although such differentiation is often difficult due to their potential overlapping features.

Uterine fibromyoma presents as a rounded formation, with homogeneous echogenicity, varying from hypoechoic to hyperechoic, based on the quantity of the smooth or connective muscle component. Less frequently they present a non-uniform echogenicity (heterogeneous), due to a mixed echogenicity or to the presence of echogenic areas or cystic areas (regular or irregular). The margins are generally clear, often hyperechoic, easily distinguishable from the surrounding myometrium. Using the color or

power Doppler it is possible to visualize a circumferential vascular flow around the lesion. They often exhibit posterior acoustic shadowing due to their dense composition and may show calcified areas, especially in older fibroids.

Sonographic findings suspicious for leiomyosarcoma may include the presence of a single large fibroma, heterogeneous echogenicity with areas of colliquative necrosis and calcifications, poorly defined and irregular borders, extensive neovascularization, especially centrally. Other sonographic findings suspicious for leiomyosarcoma may include rapid growth and invasion of adjacent organs.

MRI is included in the diagnostic pathway as a level II method. It is indicated in cases of atypical myomas due to clinical or ultrasound characteristics such as rapid growth, blood loss, pain, and atypical echostructure or vascularization.

Post-operative histological examination finally allows a definitive diagnosis. Histological features of malignancy are high mitotic activity (a mitotic index greater than 10 mitoses per 10 high-power fields), tumor necrosis, vascular invasion and nuclear atypia.

CONCLUSION

PEComas of the uterus are rare mesenchymal neoplasms that pose significant diagnostic challenges pre-operatively due to their nonspecific imaging features and no specific blood markers. These tumors often mimic other uterine masses, making accurate preoperative diagnosis difficult. Ultrasonographically, PEComas may exhibit heterogeneous echogenicity and rich vascular patterns, which can be helpful in clinical practice. In literature, there is no direct evidence of a correlation between serum levels of LDH, CA-125 and the likelihood of PEComa presence. However, we believe that these markers may nonspecifically correlate with potential malignant neoplasms. Moreover, three studies have shown that integrating serum LDH levels with various imaging techniques, such as MRI, PET-CT or FDG-PET, enhances the sensitivity and specificity of preoperative diagnoses for uterine sarcomas and myomas. The potential for malignancy in PEComas varies, with some tumors exhibiting benign behavior while others demonstrate aggressive characteristics, including local invasion and distant metastasis. Key factors indicating a higher risk of malignancy include tumor size greater than 5 cm, increased cytological and nuclear atypia, infiltration of surrounding tissues and blood vessels, presence of necrosis, and high mitotic activity. Given these complexities, a comprehensive histopathological and immunohistochemical evaluation post-surgery remains crucial for accurate diagnosis and appropriate management. This underscores the importance of including PEComa in the differential diagnosis of uterine tumors to ensure optimal surgical planning and patient outcomes. Given the rarity and complexity of PEComas, treatment should be guided by a multidisciplinary team to optimize patient outcomes and should involve oncologists, pathologists, radiologists and surgeons. The therapeutic management of PEComas requires a tailored approach, with surgical resection being the cornerstone of treatment. Adjuvant therapies, particularly mTOR inhibitors, offer additional options for managing advanced or high-risk cases.

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